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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,773	06/21/2001	William Butler Cowden	120081.403C1	9179

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/27/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/887,773	Cowden et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 5, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *22-24 and 26-29* ~~is~~/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *22-24 and 26-29* ~~is~~/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 12/05/02 (paper no. 7) in response to the non-final Office Action mailed 06/19/02 (paper no. 5). With this, Applicants have amended the specification. The amendment introduced at line 13 on page 18 of the specification appears to be out of order/place.

Status of Claims

2) Claim 25 has been canceled via the amendment filed 12/05/02.

Claims 22-24 and 26-28 have been amended via the amendment filed 12/05/02.

Claim 29 has been added via the amendment filed 12/05/02.

Claims 22-24 and 26-29 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

5) The objection to the specification made in paragraph 6 of the Office Action mailed 06/19/02 (paper no. 5) is maintained. The section: "Brief Description of the Drawing" is still missing in the instant specification, for example, at line 13 on page 18.

Rejection(s) Moot

6) The rejection of claim 25 made in paragraph 8 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

7) The rejection of claim 25 made in paragraph 9 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, first paragraph, as being non-enabled, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 25 made in paragraph 11 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 102(b) as being anticipated by Zhang *et al.* (*Acta Virologica* 38: 327-332, 1994), or Gajdosova *et al.* (*Acta Virologica* 38: 339-344, 1994), or Williams *et al.* (*Infect. Immun.* 51: 851-858, 1986) as evidenced by Levy *et al.* (*Eur. J. Epidemiol.* 5: 447-453, 1989, abstract), or Roue *et al.* (*Lancet* 341: 1094-1095, 1993), is moot in light of Applicants' cancellation of the claim.

9) The rejection of claim 25 made in paragraph 12 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 102(b) as being anticipated by Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) as evidenced by Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988) and Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995), is moot in light of Applicants' cancellation of the claim.

10) The rejection of claim 25 made in paragraph 14 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 103(a) as being unpatentable over Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) in view of Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988), Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995) and Barnes *et al.* (WO 87/06590), moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

11) The rejection of claims 22-24 and 26-28 made in paragraph 8(a) of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

12) The rejection of claims 24 and 28 made in paragraph 8(c) of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

13) The rejection of claim 22 made in paragraph 8(d) of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

Rejection(s) Maintained

14) The rejection of claim 22 made in paragraph 8(b) of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

Applicants contend that one of skill in the art would fully understand the term "analogous or homologous" from the extensive definition at line 7 of page 7 through line 26 of page 9 to be components that are structurally or functionally similar to such components as *C. burnetii,* and are able to inhibit, delay or ameliorate autoimmune disease in a mammal.

Applicants' arguments have been carefully considered, but are non-persuasive. Since the parameters for determining the analogy or homology of one antigenic component relative to another are not defined, it is not clear what constitutes analogous or homologous components. It is unclear which characteristics an antigen should have in order to qualify as an "analogous or homologous" antigenic component, or what degree of analogy or homology should an antigen show in order to qualify as an "analogous or homologous" antigenic component. Does a polypeptide having 1% or 2% sequence homology with a polypeptide of *C. burnetii* qualify as an 'analogous or homologous component' as recited?

15) The rejection of claims 23-24 and 26-28 made in paragraph 8(e) of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reason set forth therein.

New claim 29, which depends from claims 26 and 29, is now added to this rejection.

16) The rejection of claims 22-24 and 26-28 made in paragraph 9 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 112, first paragraph, as being non-enabled, is maintained for reasons set forth therein and herebelow.

New claim 29, which depends from claims 26 and 22, is now added to this rejection.

Applicants contend that claims 22-28 have been amended for clarification. Applicants state that amended claims 22-28 read on antigenic components of *Coxiella burnetii*, or analogous or homologous components, and that they are fully enabled by the instant specification. Applicants submit that support for such components can be found in Examples 1-5, pages 19-24 as well as at lines 16-20 of page 6 and lines 10-20 of page 7. Applicants assert that routine experimentation of generating polyclonal and monoclonal antibodies in a laboratory animal from bacterial components or whole cell lysates may require a fair amount of time, but not considerable skill. Applicants assert that generating antibodies from bacterial components is standard practice.

Applicants' arguments have been carefully considered, but are non-persuasive. In the instant

case, the nature of the invention is related to the use of one or more antigenic component(s) of *Coxiella burnetii*, or antigenic components "analogous or homologous" to one or more antigenic components of *Coxiella burnetii* in the manufacture of a medicament for the treatment of an autoimmune disease, IDDM in particular. The breadth of the claims encompasses the use of any antigenic components, isolated as well as non-isolated components, that are analogous or homologous to one or more antigenic components of *Coxiella burnetii,* for use in the claimed method against any autoimmune disease. The one or more 'analogous or homologous antigenic components thereof' can be of any origin, microbial, non-microbial, or of host cell origin. However, other than QFA antigen or QVAX of *Coxiella burnetii*, no other components analogous or homologous to the antigenic components of *Coxiella burnetii*, are identified and enabled for use in the manufacture of the medicament. The only working examples are directed to QFA and QVAX, both art-known products of *Coxiella burnetii*. Without a specific teaching in the specification, as originally filed, of the parameters for determining the analogy or homology of one antigenic component relative to another, what constitutes analogous or homologous antigenic components cannot be envisaged. *C. burnetii* contains and produces a plethora of antigens, immunogenic and non-immunogenic, or therapeutic and non-therapeutic. Which characteristics an antigen or a component should have in order to qualify as an "analogous or homologous" antigenic component, or what degree of analogy or homology should an antigen or component show in order to qualify as an "analogous or homologous" antigenic component is not taught. For example, if one viewed a microbial or non-microbial polypeptide having 1% or 2% structural or sequence homology to an isolated polypeptide of *C. burnetii* as meeting the claim limitation of 'analogous or homologous component', would such an antigen component have the same autoimmune-therapeutic function as the native antigen of *C. burnetii*? In the instant case, undue experimentation would have been required: a) first to figure out what components, such as, proteins, peptides, lipids, glycoproteins, carbohydrates or mixtures thereof etc., qualify as antigenic analogues or homologues as recited; b) then to determine what extent of analogy or homology to an unspecified antigen is required to qualify as an analogous or homologous antigenic component; c) then to identify or isolate such antigenic analogues or homologues; and d) then to evaluate the antigenic analogues or homologues for their therapeutic efficacy against a myriad of mammalian autoimmune diseases that are currently

encompassed in the scope of the claims. The ability to reproducibly practice the full scope of the claimed method is well outside the realm of routine experimentation. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

17) The rejection of claims 22, 23 and 26-28 made in paragraph 11 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 102(b) as being anticipated by Zhang *et al.* (*Acta Virologica* 38: 327-332, 1994), or Gajdosova *et al.* (*Acta Virologica* 38: 339-344, 1994), or Williams *et al.* (*Infect. Immun.* 51: 851-858, 1986) as evidenced by Levy *et al.* (*Eur. J. Epidemiol.* 5: 447-453, 1989, abstract), or Roue *et al.* (*Lancet* 341: 1094-1095, 1993), is maintained for reasons set forth therein and herebelow.

Applicants cite case law and contend that none of the prior art reference expressly or inherently describes a method of using one or more antigenic components of *Coxiella burnetii* in the manufacture of a medicament for treatment of autoimmune disease in a mammal. Applicants submit that the prior art references do not disclose any information related to treatment of autoimmune disease in a mammal.

Applicants' arguments have been carefully considered, but are non-persuasive. As set forth in paragraph 11 of the Office Action mailed 06/19/02 (paper no. 5), Zhang *et al.*, Gajdosova *et al.*, or Williams *et al.* taught the claimed process. It should be noted that the preamble in claim 22: "for the treatment of an autoimmune disease in a mammal" merely represents the purpose, or the intended use of the medicament or antigenic components used in the claimed method. Such a recitation is not given any patentable weight unless Applicants show that it results in a manipulative difference between the claimed process and the prior art. The rejection stands.

18) The rejection of claims 22-24 and 26-28 made in paragraph 12 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 102(b) as being anticipated by Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) as evidenced by Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988) and Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995), is maintained for reasons set forth therein and herebelow.

Applicants contend that the presently claimed invention reads on a method for using antigenic components of *C. burnetii,* or analogous or homologous components in the manufacture of a medicament for treatment of autoimmune disease in a mammal, which is not disclosed in any of the

cited prior art references. Applicants submit that the prior art references read on general adjuvants, which is recognized by one of skill in the art to contain many components that may amplify any general immunological reaction. Applicants further state that immunostimulation of non-obese diabetic mice by complete Freund's adjuvant does not completely block the autoimmune response, instead coverts the response from a destructive into a non-destructive form of auto-immunity. Applicants assert that complete Freund's adjuvant does not prevent or reverse autoimmunity directed against islet tissue in diabetic mice. Applicants point to parts of the specification and explain how QFA is more efficacious than complete Freund's adjuvant and how the instant invention fulfills the long-felt need in the art for an agent capable of blocking autoimmune disease without the side effects that occur with treatment of complete Freund's adjuvant.

Applicants' arguments have been carefully considered, but are non-persuasive. Applicants are reminded that the instant claims are not directed to a method of completely blocking an autoimmune response, or to a method of preventing or reversing autoimmunity directed against islet tissue in diabetic mice, or to a method of blocking the side effects that occur with the use of complete Freund's adjuvant. Instead, the claims are drawn to a method of use of one or more *C. burnetii* antigenic components in the manufacture of a medicament. As set forth in detail in paragraph 12 of the Office Action mailed 06/19/02 (paper no. 5), the cited prior art taught such a method.

19) The rejection of claims 22-24 and 26-28 made in paragraph 14 of the Office Action mailed 06/19/02 (paper no. 5) under 35 U.S.C § 103(a) as being unpatentable over Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) in view of Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988), Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995) and Barnes *et al.* (WO 87/06590), is maintained for reasons set forth therein and herebelow.

Applicants cite case law and contend that the Office has failed to establish a *prima facie* case of obviousness because nothing in the cited prior art provides the desirability or motivation for one of skill in the art to combine the relevant teachings of the cited prior art. Applicants submit that Qin *et al.* and Vodkin *et al.* fail to teach or suggest a 'method of antigenic components of more *C. burnetii* or analogous or homologous components used in the manufacture of a medicament for treatment of autoimmune disease in a mammal'. Applicants state that Edgington's teaching is

unrelated to the presently claimed invention. Applicants submit that the presently claimed invention is more efficacious than other methods presently known in the art 'for delaying or inhibiting autoimmune disease, and provides the significant benefit of the lack of skin lesions at the site of injection. Applicants allege that Barnes *et al.* is an 'obvious to try' disclosure.

Applicants' arguments have been carefully considered, but are non-persuasive. Applicants are reminded that the instant claims are not directed to a more efficacious method of delaying or inhibiting an autoimmune disease, or to a method of preventing of skin lesions at the site of injection. Instead, the claims are drawn to a method of use of one or more *C. burnetii* antigenic components in the manufacture of a medicament. The cited references are applied under 35 U.S.C § 103, and not under 35 U.S.C § 102. As set forth in detail in paragraph 14 of the Office Action mailed 06/19/02 (paper no. 5), the cited prior art references collectively taught the claimed method. The motivation to replace Qin's CFA with Vodkin's analogous immunogenic *Coxiella burnetii* HSP antigenic component in Qin's method of making comes from the express teaching of Barnes who taught the CFA adjuvant to be unsatisfactory for use in humans, pets and in meat animals due to the undesired side effects. The rejection stands.

New Rejection(s)

Applicants are asked to note the following new rejection(s) made in this Office Action. The new rejections are necessitated by Applicants' amendments to the claims and/or Applicants' addition of new claim(s).

Rejection(s) under 35 U.S.C § 112, Second Paragraph

20) Claim 29 is rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 29 is incomplete and lacks a period at the end.

(b) Claim 29 is confusing in the recitation "antigenic component is a Q fever vaccine (QVAX". The commercially available QVAX is known to comprise whole cells of *C. burnetii*, but not any components therefrom. See the disclosure of Izzo *et al.* (1991) below. Furthermore, it is unclear how one can use an already manufactured commercial QVAX vaccine in the 'manufacture' of a medicament. Clarification/correction is requested.

Rejection(s) under 35 U.S.C § 102

21) Claims 22, 23, 26 and 29 are rejected under 35 U.S.C § 102(b) as being anticipated by Izzo *et al.* (*Clin. Exp. Immunol.* 85: 98-108, 1991) (Izzo *et al.*, 1991) or Izzo *et al.* (*J. Infect. Dis.* 157: 781-789, 1988) (Izzo *et al.*, 1988).

The preamble recitation in the base claim: "for the treatment of an autoimmune disease in a mammal" merely represents the purpose or the intended use of the medicament or antigenic components used in the claimed method, and therefore is not given any patentable weight.

Izzo *et al.* (1991) taught a method of using Q-VAX, a formalin-inactivated whole cell *C. burnetii* vaccine, in the production of a medicament (see under 'Subjects and Methods' and page 98).

Izzo *et al.* (1988) taught a method of using a *C. burnetii* phase-I antigen-containing Q fever vaccine in the production of a medicament (see under 'Subjects and Methods', especially under the subsection 'Antigens').

Claims 22, 23, 26 and 29 anticipated by Izzo *et al.* (1991) or Izzo *et al.* (1988).

Remarks

22) Claims 22-24 and 26-29 stand rejected.

It is noted that in claim 28, the limitation "**the** Q fever antigen" has improper antecedence [Emphasis added]. Claim 22 improperly includes an incomplete parenthesis in line 3 of the claim, whereas claim 29 is missing a part of the parenthesis.

23) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

24) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

25) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

February, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER